IN THE SPECIFICATION

It is noted that the application does not contain an abstract. Applicant forwards herewith p. 57 of the application which contains the "Abstract of the Invention".

Please replace the paragraph beginning on page 1, line 1, after the title, with the following rewritten paragraph:

This application is a continuation of application Serial No. 08/880,855, filed June 23, 1997, now abandoned, which is a continuation-in-part of application Serial No. 08/842,842, filed April 16, 1997, now U.S. Patent No. 5,843,678, which is hereby incorporated by reference.

Please replace the paragraph beginning on page 1, line 31, with the following paragraph:

Osteoclasts are large phagocytic ~~mutinucleated~~ multinucleated cells which are formed from hematopoietic precursor cells in the bone marrow. Although the growth and formation of mature functional osteoclasts is not well understood, it is thought that osteoclasts mature along the monocyte/macrophage cell lineage in response to exposure to various growth-promoting factors. Early development of bone marrow precursor cells to preosteoclasts are believed to mediated by soluble factors such as tumor necrosis factor-α (TNF-α), tumor necrosis factor-β (TNF-β), interleukin-1 (IL-1), interleukin-4 (IL-4), interleukin-6 (IL-6), and leukemia inhibitory factor (LIF). In culture, preosteoclasts are formed in the presence of added macrophage colony stimulating factor (M-CSF). These factors act primarily in early steps of osteoclast development. The involvement of polypeptide factors in terminal stages of osteoclast formation has not been extensively reported.

It has been reported, however, that parathyroid hormone stimulates the formation and activity of osteoclasts and that calcitonin has the opposite effect, although to a lesser extent.

Please replace the paragraph beginning on page 2, line 19, with the following paragraph:

Recently, a new polypeptide factor, termed osteoprotegerin (OPG), has been described which negatively regulated formation of osteoclasts in vitro and in vivo (see co-owned and co-pending U.S. Serial Nos. 08/577,788 filed December 22, 1995, 08/706,945 filed September 3, 1996, and 08/771,777, filed December 20, 1996, now abandoned, hereby incorporated by reference; and PCT Application No. WO96/26271). OPG dramatically increased the bone density in transgenic mice expressing the OPG polypeptide and reduced the extent of bone loss when administered to ovariectomized rats. An analysis of OPG activity in in vitro osteoclast formation revealed that OPG does not interfere with the growth and differentiation of monocyte/macrophage precursors, but more likely blocks the differentiation of osteoclasts from monocyte/macrophage precursors. Thus OPG appears to have specificity in regulating the extent of osteoclast formation.

Please replace the paragraph beginning on page 4, line 35, with the following paragraph:

Figure 1. (SEQ ID NO:36 and 37) Structure and sequence of the 32D-F3 insert encoding OPG binding protein. Predicted transmembrane domain and sites for asparagine-linked carbohydrate chains are underlined.

Please replace the paragraph beginning on page 5, line 26, with the following paragraph:

Figure 4. (SEQ ID NO:38 and 39) Structure and sequence of the pcDNA/ hu OPGbp 1.1 insert encoding the human OPG binding protein. The predicted transmembrane domain and site for asparagine-linked carbohydrate chains are underlined.

Please replace the paragraph beginning on page 5, line 32, with the following paragraph:

Figure 5. Stimulation of osteoclast development in vitro from bone marrow macrophage and ST2 cell cocultures treated with recombinant murine OPG binding protein [158-316]. Cultures were treated with varying concentrations of murine OPG binding protein ranging from 1.6 to 500 ng/ml (—✱—). After 8-10 days, cultures were lysed, and TRAP activity was measured by solution assay. In addition, some cultures were simultaneously treated with 1 (—◇—), 10 (—⊠—), 100 —△—), 500 (—□—), and 1000 ng/ml (—○—) of recombinant murine OPG [22-401]-Fc protein. Murine OPG binding protein induces a dose-dependent stimulation in osteoclast formation, whereas OPG [22-401]-Fc inhibits osteoclast formation.

Please replace the paragraph beginning on page 6, line 10, with the following paragraph:

Figure 6. Stimulation of osteoclast development from bone marrow precursors in vitro in the presence of M-CSF and murine OPG binding protein [158-316]. Mouse bone marrow was harvested, and cultured in the presence 250 (—◇—), 500 (—□—), 1000 (—△—), and 2000 U/ml (—○—) of M-CSF. Varying concentrations of OPG binding protein [158-316], ranging from 1.6 to 500 ng/ml, were added to these same cultures. Osteoclast development was measured by TRAP solution assay.

Please replace the paragraph beginning on page 7, line 21, with the following paragraph:

The invention provides for a polypeptide referred to as an OPG binding protein, which specifically binds OPG and is involved in osteoclast differentiation. A cDNA clone encoding the murine form of the polypeptide was identified from a library prepared from a mouse myelomonocytic cell line 32-D and transfected into COS cells. Transfectants were screened for their ability to bind to an OPG[22-201]-Fc fusion polypeptide (Example 1). The nucleic acid sequence revealed that OPG binding protein is a novel member of the TNF family and is most closely related to AGP-1, a polypeptide previously described in co-owned and co-pending U.S. Serial No. 08/660,562, filed June 7, 1996, now abandoned. (A polypeptide identical to AGP-1 and designated TRAIL is described in Wiley et al. Immunity 3, 673-682 (1995)). OPG binding protein is predicted to be a type II transmembrane protein having a cytoplamsic domain at the amino terminus, a transmembrane domain, and a carboxy terminal extracellular domain (Figure 1). The amino terminal cytoplasmic domain spans about residues 1-48, the transmembrane domain spans about residues 49-69 and the extracellular domain spans about residues 70-316 as shown in Figure 1 (SEQ ID NO:37). The membrane-associated protein specifically binds OPG (Figure 2). Thus OPG binding protein and OPG share many characteristics of a receptor-ligand pair although it is possible that other naturally-occurring receptors for OPG binding protein exist.